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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
CARLSON, K

ART UNIT	PAPER NUMBER
1812	14

DATE MAILED: 07/22/92

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

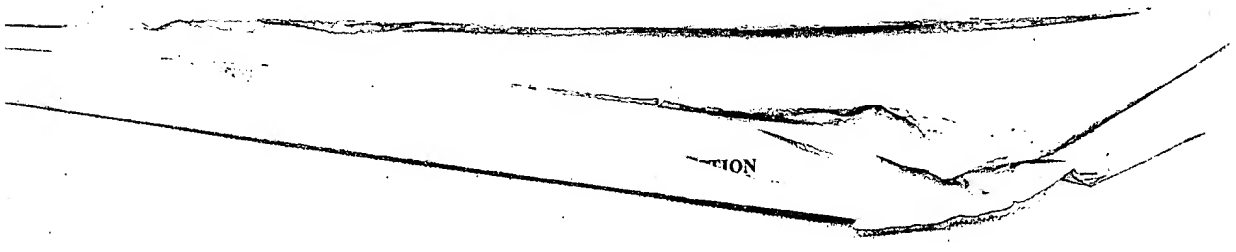
A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-9 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-9 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____; has been ☐ approved. ☐ disapproved (see explanation).
12. ☒ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other



The priority date for this application has been set to July 12, 1990. This date has been chosen because Israel Patent 092697 filed December 13, 1989 does not claim or demonstrate enablement of the method for the production of TNF-BP via recombinant techniques. Israel Patent 095064 filed July 12, 1990 does claim the method and enablement is demonstrated in Example 2, page 25.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the title of the invention, each of the lettered items should be preceded by the headings indicated below.

(a) Title of the Invention.
(b) Cross-References to Related Applications (if any).
(c) Statement as to rights to inventions made under Federally-sponsored research and development (if any).
(d) Background of the invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 C.F.R. §§ 1.97-1.99.
(e) Summary of the Invention.
(f) Brief Description of the Drawing.

(g) Description of the Preferred Embodiment(s).
(h) Claim(s).
(i) Abstract of the Disclosure.

The Applicants have not cross-referenced the patent application Serial Number 07/243092 as being the parent application to the instant application. The Applicants should amend the specification in such a manner that Serial Number 07/243092 and it relation to the current application is explained in the first paragraph of the specification.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, and 6-8 are rejected under 35 U.S.C. § 102(a) as being anticipated by Loetscher et al. (April 20, 1990) or Schall et al. (April 20, 1990). Loetscher et al. teach the expression of TNF-BP from HL60, U937, AG1523, HEp2, and COS cells (page 354). Loetscher et al. express TNF-BP that is 100% identical to that of the Applicants (Fig. 1) from two expression systems, a cytomegalovirus immediate-early promoter followed by an SV40 termination signal expression system and a baculovirus expression system. Schall et al. also teach the expression of TNF-BP that is identical to the Applicants from several varied cell types that include hepatocytes, breast carcinoma cells, and glioblastoma cells. Therefore, the method for the production of

TNF-BP from eukaryotic cells and the TNF-BP protein so produced has been taught in the prior art.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 3 and 4 are rejected under 35 U.S.C. § 103 as being unpatentable over Loetscher et al. or Schall et al. in view of Sambrook et al (1988). The teachings of Loetscher et al. and Schall et al. have been explained in the 35 USC 102 rejection of Claims 1, 2, and 6-8 above. Loetscher et al. further teaches the detection of TNF-BP via the use of monoclonal antibodies. Sambrook et al. teaches the use of the dhfr amplification system in dhfr-deficient CHO cells for the expression of proteins under the influence of methotrexate (page 16.28). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to express TNF-BP in dhfr deficient CHO cells under the dhfr promoter because Loetscher et al. or Schall et al. teach the expression of TNF-BP in several different cell

types under several different promoters and Sambrook et al. teaches the use of dhfr expression system in dhfr-deficient CHO cells to express proteins. It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect the released TNF-BP using antibodies because Loetscher et al. teaches the use of antibodies to detect TNF-BP that has been recombinantly expressed.

Claims 5 and 9 are rejected under 35 U.S.C. § 103 as being unpatentable over Loetscher et al. or Schall et al. Loetscher et al. and Schall et al. teach the protein sequence for TNF-BP. Because it is identical to that of the Applicants, analysis the TNF-BP disclosed by Loetscher et al. or Schall et al. by reverse phase HPLC should result in the same retention time as that observed by the Applicants. It would have been obvious to one of ordinary skill in the art at the time the invention was made that the TNF-BP disclosed by Loetscher et al. or Schall et al. would have the same retention time observed after reverse phase HPLC analysis as that of the Applicant's because the TNF-BPs are identical and Claim 5 is rejected accordingly. Claim 9 is rejected because, Loetscher et al. or Schall et al. expressed TNF-BP in numerous cell lines. Therein, it would have been obvious to one of ordinary skill in the art at the time the invention was made that reasonable success in recombinantly producing the protein claimed could be expected if CHO cells were transformed with DNA encoding TNF-BP.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide and enabling disclosure. The specification does not enable all analogs of TNF-BP, nor the preparation of such.

Claims 1-9 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 1 and 8 it is not clear what a soluble TNF-BP precursor or analog is. For example, is the precursor the membrane-bound TNF receptor? The term "analog" is broad and indefinite and should be defined in view of the enablement of the specification (see above). In Claims 1, 2, and 8 it is not clear what the Applicants mean when they describe the TNF receptor as being the "whole" receptor. That is, does the "whole" TNF receptor include the precursor form of the protein or post-translational modifications? Or does "whole" encompass only the extracellular, transmembrane, and cytoplasmic regions - the mature protein? Claims 8 and 9 recite "soluble protein" in the

preamble of the claims which is contradictory to the rest of the claim that refers to the "whole" receptor. "Soluble protein" typically refers to that portion of the receptor that is exclusive of the transmembrane and cytoplasmic domains and not considered to the "whole" or the "mature" protein.

Any inquiry concerning this communication should be directed to Karen Cochrane Carlson, Ph.D. at telephone number (703) 305-7811.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GARNETTE D. DRAPER
PRIMARY EXAMINER
ART UNIT ~~186~~ 1812